

WHAT IS CLAIMED IS:

1. A BChE derived peptide capable of preventing and/or reversing amyloid fibril formation.
2. The BChE derived peptide of claim 1, selected from the group consisting of SEQ ID NOs:1 and 8-20302.
3. A pharmaceutical composition comprising as an active ingredient BChE or a BChE derived peptide, said peptide being capable of preventing and/or reversing amyloid fibril formation and a pharmaceutically acceptable carrier.
4. The pharmaceutical composition of claim 3, wherein said BChE derived peptide is selected from the group consisting of SEQ ID NOs:1 and 8-20302.
5. The pharmaceutical composition of claim 3, wherein said BChE derived peptide is set forth by SEQ ID NO:1.
6. The pharmaceutical composition of claim 3, wherein said active ingredient is formulated in a therapeutically effective amount providable at a dose range of 0.1 – 1000 micromol per kg body weight.
7. The pharmaceutical composition of claim 3, wherein said active ingredient is formulated in a therapeutically effective amount providable at a dose range of 1-100 micromol per kg body weight.
8. The pharmaceutical composition of claim 3, wherein said active ingredient is formulated in a therapeutically effective amount providable at a dose range of 5-50 micromol per kg body weight.
9. The pharmaceutical composition of claim 3, wherein said pharmaceutically acceptable carrier is selected for reducing an immunogenicity of said peptide.

10. The pharmaceutical composition of claim 3, wherein said pharmaceutically acceptable carrier is selected for sustained release of said peptide.

11. A method of treating an individual having or being predisposed to a disease or disorder associated with amyloid fibril formation, the method comprising administering to the individual a therapeutically effective amount of BChE or BChE derived peptide, thereby treating the individual having or being predisposed to a disease or disorder associated with amyloid fibril formation.

12. The method of claim 11, wherein said BChE derived peptide is selected from the group consisting of SEQ ID NO:1 and 8-20302.

13. The method of claim 11, wherein said disease or disorder associated with amyloid fibril formation is selected from the group consisting of a neurodegenerative disease, a disorder associated with systemic amyloidosis, a disorder associated with localized amyloidosis, a prion disease and/or a polyglutamine disorder.

14. The method of claim 13, wherein said neurodegenerative disease is selected from the group consisting of Alzheimer's disease, Huntington's disease and Parkinson's disease.

15. The method of claim 13, wherein said disorder associated with systemic amyloidosis is selected from the group consisting of Multiple myeloma, Chronic inflammatory disease, Rheumatoid arthritis, Tuberculosis, Skin abscess, lung abscess, Cancer, Hodgkin's disease, Hemodialysis for chronic renal failure, Heredofamilial amyloidosis, Familial Mediterranean Fever and Familial amyloid polyneuropathy.

16. The method of claim 13, wherein said disorder associated with localized amyloidosis is selected from the group consisting of Senile cardiac amyloidosis, Senile cerebral amyloidosis, Endocrine tumors, Medullary carcinoma of thyroid, Type II diabetes and Pancreatic islets β -cells.

17. The method of claim 13, wherein said prion disease is selected from the group consisting of Creutzfeldt-Jakob disease (CJD), spongiform encephalopathies (TSE's), mad cow disease, Gerstmann-Straussler-Scheinker disease (GSS) and Kuru.

18. The method of claim 13, wherein said polyglutamine disorder is selected from the group consisting of Huntington's disease (HD), Spinal and Bulbar Muscular Atrophy (SBMA), DentatoRubral and PallidoLuisian Atrophy (DRPLA), spinocerebellar ataxia type 1 (SCA1), spinocerebellar ataxia type 2 (SCA2), Spinocerebellar ataxia type-3 (SCA3; Machado-Joseph Disease), Spinocerebellar ataxia type 7 (SCA7) and Spinocerebellar ataxia type 17 (SCA17).

19. The method of claim 11, wherein said amyloid is a protein selected from the group consisting of Transthyretin, Amyloid beta protein, Procalcitonin, IAPP (Amylin), amyloid light chain (AL), non-immunoglobulin amyloid associated (AA), non-immunoglobulin amyloid associated serum precursor (SAA), α -synucleic protein, ataxin and huntingtin.

20. The method of claim 11, wherein said peptide is set forth by SEQ ID NO:1.

21. The method of claim 11, wherein said therapeutically effective amount is providable at a dose range of 0.1 – 1000 micromol per kg body weight.

22. The method of claim 11, wherein said therapeutically effective amount is providable at a dose range of 1-100 micromol per kg body weight.

23. The method of claim 11, wherein said therapeutically effective amount is providable at a dose range of 5-50 micromol per kg body weight.

24. A method of identifying a BChE derived peptide capable of preventing and/or reversing amyloid fibril formation comprising contacting the BChE derived

peptide with an amyloid precursor protein and a β -sheet – responsive dye and measuring a fluorescence intensity resulting from said β -sheet – responsive dye prior to and following said contacting said BChE derived peptide with said amyloid precursor protein, wherein delayed or reduced increase in said fluorescence intensity following said contacting said BChE derived peptide with said amyloid precursor protein is indicative of an ability of the peptide to prevent amyloid fibril formation.

25. The method of claim 24, wherein said BChE derived peptide is selected from the group consisting of SEQ ID NOs:8-20302.

26. The method of claim 24, wherein said β -sheet – responsive dye is a benzothiazole dye.

27. The method of claim 24, wherein said β -sheet – responsive dye is Thioflavin T.

28. The method of claim 27, wherein said Thioflavin T is provided at a concentration range of 0.5-1.5 μ M.

29. The method of claim 27, wherein said Thioflavin T is provided at a concentration of about 1 μ M.

30. The method of claim 24, wherein said amyloid precursor protein is selected from the group consisting of Transthyretin, Amyloid beta protein, Amyloid beta (1-40), Procalcitonin, IAPP (Amylin), amyloid light chain (AL), non-immunoglobulin amyloid associated (AA), non-immunoglobulin amyloid associated serum precursor (SAA), α -synucleic protein, ataxin and huntingtin.

31. The method of claim 30, wherein said Amyloid beta (1-40) is provided at a concentration in the range of 20-50 μ M.

32. The method of claim 30, wherein said Amyloid beta (1-40) is provided at a concentration of about 33 μ M.

33. A method of preventing and/or reversing amyloid fibril formation in a tissue of an individual comprising increasing a level of BChE or a BChE derived peptide being capable of preventing and/or reversing amyloid fibril formation in the tissue, thereby preventing and/or reversing amyloid fibril formation therein.

34. The method of claim 33, wherein the tissue is of an individual having, or being predisposed to an amyloid fibril-associated disease or disorder.

35. The method of claim 34, wherein said individual has a neurodegenerative disease, a disorder associated with systemic amyloidosis, a disorder associated with localized amyloidosis, a prion disease and/or a polyglutamine disorder.

36. The method of claim 35, wherein said neurodegenerative disease is selected from the group consisting of Alzheimer's disease, Huntington's disease and Parkinson's disease.

37. The method of claim 35, wherein said disorder associated with systemic amyloidosis is selected from the group consisting of Multiple myeloma, Chronic inflammatory disease, Rheumatoid arthritis, Tuberculosis, Skin abscess, lung abscess, Cancer, Hodgkin's disease, Hemodialysis for chronic renal failure, Heredofamilial amyloidosis, Familial Mediterranean Fever and Familial amyloid polyneuropathy.

38. The method of claim 35, wherein said disorder associated with localized amyloidosis is selected from the group consisting of Senile cardiac amyloidosis, Senile cerebral amyloidosis, Endocrine tumors, Medullary carcinoma of thyroid, Type II diabetes and Pancreatic islets β -cells.

39. The method of claim 35, wherein said prion disease is selected from the group consisting of Creutzfeldt-Jakob disease (CJD), spongiform encephalopathies (TSE's), mad cow disease, Gerstmann-Straussler-Scheinker disease (GSS) and Kuru.

40. The method of claim 35, wherein said polyglutamine disorder is selected from the group consisting of Huntington's disease (HD), Spinal and Bulbar Muscular Atrophy (SBMA), DentatoRubral and PallidoLuysian Atrophy (DRPLA), spinocerebellar ataxia type 1 (SCA1), spinocerebellar ataxia type 2 (SCA2), Spinocerebellar ataxia type-3 (SCA3; Machado-Joseph Disease), Spinocerebellar ataxia type 7 (SCA7) and Spinocerebellar ataxia type 17 (SCA17).

41. The method of claim 33, wherein said amyloid is a protein selected from the group consisting of Transthyretin, Amyloid beta protein, Procalcitonin, IAPP (Amylin), amyloid light chain (AL), non-immunoglobulin amyloid associated (AA), non-immunoglobulin amyloid associated serum precursor (SAA), α -synucleic protein, ataxin and huntingtin.

42. The method of claim 33, wherein said increasing is effected by at least one approach selected from the group consisting of:

- (a) expressing in cells of the individual an exogenous polynucleotide encoding said BChE or said BChE derived peptide;
 - (b) increasing expression of endogenous BChE in the individual;
 - (c) increasing endogenous BChE activity in the individual;
 - (d) administering BChE or the BChE derived peptide to the individual;
- and
- (e) administering to the individual cells expressing the BChE or the BChE derived peptide.

43. The method of claim 42, wherein said exogenous polynucleotide encoding said BChE or said BChE derived peptide is derived from SEQ ID NO:7.

44. The method of claim 42, wherein said BChE is as set forth in SEQ ID NO:2.

45. The method of claim 42, wherein said BChE derived peptide is as set forth in any of SEQ ID NOs:1 and 8-20302.

46. A method of treating an individual having or being predisposed to a disease or disorder associated with amyloid fibril formation, the method comprising increasing a level of BChE or a BChE derived peptide in a tissue susceptible to the amyloid fibril formation of the individual, thereby treating the individual having or being predisposed to a disorder associated with amyloid fibril formation.

47. The method of claim 46, wherein said disease or disorder associated with amyloid fibril formation is a neurodegenerative disease, a disorder associated with systemic amyloidosis, a disorder associated with localized amyloidosis, a prion disease and/or a polyglutamine disorder.

48. The method of claim 47, wherein said neurodegenerative disease is selected from the group consisting of Alzheimer's disease, Huntington's disease and Parkinson's disease.

49. The method of claim 47, wherein said disorder associated with systemic amyloidosis is selected from the group consisting of Multiple myeloma, Chronic inflammatory disease, Rheumatoid arthritis, Tuberculosis, Skin abscess, lung abscess, Cancer, Hodgkin's disease, Hemodialysis for chronic renal failure, Heredofamilial amyloidosis, Familial Mediterranean Fever and Familial amyloid polyneuropathy.

50. The method of claim 47, wherein said disorder associated with localized amyloidosis is selected from the group consisting of Senile cardiac amyloidosis, Senile cerebral amyloidosis, Endocrine tumors, Medullary carcinoma of thyroid, Type II diabetes and Pancreatic islets β -cells.

51. The method of claim 47, wherein said prion disease is selected from the group consisting of Creutzfeldt-Jakob disease (CJD), spongiform encephalopathies (TSE's), mad cow disease, Gerstmann-Straussler-Scheinker disease (GSS) and Kuru.

52. The method of claim 47, wherein said polyglutamine disorder is selected from the group consisting of Huntington's disease (HD), Spinal and Bulbar Muscular Atrophy (SBMA), DentatoRubral and PallidoLusian Atrophy (DRPLA), spinocerebellar ataxia type 1 (SCA1), spinocerebellar ataxia type 2 (SCA2), Spinocerebellar ataxia type-3 (SCA3; Machado-Joseph Disease), Spinocerebellar ataxia type 7 (SCA7) and Spinocerebellar ataxia type 17 (SCA17).

53. The method of claim 46, wherein said amyloid is a protein selected from the group consisting of Transthyretin, Amyloid beta protein, Procalcitonin, IAPP (Amylin), amyloid light chain (AL), non-immunoglobulin amyloid associated (AA), non-immunoglobulin amyloid associated serum precursor (SAA), α -synucleic protein, ataxin and huntingtin.

54. The method of claim 46, wherein said increasing is effected by at least one approach selected from the group consisting of:

- (a) expressing in cells of the individual an exogenous polynucleotide encoding said BChE or said BChE derived peptide;
 - (b) increasing expression of endogenous BChE in the individual;
 - (c) increasing endogenous BChE activity in the individual;
 - (d) administering BChE or the BChE derived peptide to the individual;
- and
- (e) administering to the individual cells expressing the BChE or the BChE derived peptide.

55. The method of claim 54, wherein said exogenous polynucleotide encoding said BChE or said BChE derived peptide is derived from SEQ ID NO:7.

56. The method of claim 54, wherein said BChE is as set forth in SEQ ID NO:2.

57. The method of claim 54, wherein said BChE derived peptide is as set forth in any of SEQ ID NOs:1 and 8-20302.

58. A method of limiting or reducing an inflammatory reaction in an individual, comprising increasing an expression level and/or activity of BChE in the individual, thereby limiting or reducing the inflammatory reaction in the individual.

59. The method of claim 58, wherein the inflammatory reaction is modulated by circulating acetylcholine.

60. The method of claim 58, wherein said individual is subjected to a surgery, stress or a trauma.

61. The method of claim 58, wherein the inflammatory reaction is mediated by at least one pro-inflammatory cytokine selected from the group consisting of IL-1, IL-1 α , IL-1 β , IL-1ss, IL-6, IL-8, IL-10, IL-12, IL-18 and TNF α .

62. The method of claim 58, wherein said increasing is effected by at least one approach selected from the group consisting of:

- (a) expressing in cells of the individual an exogenous polynucleotide encoding at least a functional portion of BChE;
- (b) increasing expression of endogenous BChE in the individual;
- (c) increasing endogenous BChE activity in the individual;
- (d) administering an exogenous polypeptide including at least a functional portion of BChE to the individual;
- (e) administering cells expressing the BChE into said individual.

63. The method of claim 62, wherein said exogenous polynucleotide encoding at least a functional portion of BChE is set forth by SEQ ID NO:7.

64. The method of claim 62, wherein said BChE is set forth by SEQ ID NO:2.

65. The use of BChE or a BChE derived peptide in the manufacturing of a medicament for the treatment of a disease or disorder associated with amyloid fibril formation or a predisposition thereto.

66. The use of claim 65, wherein said BChE derived peptide is selected from the group consisting of SEQ ID NO:1 and 8-20302.

67. The use of claim 65, wherein said disease or disorder associated with amyloid fibril formation is selected from the group consisting of a neurodegenerative disease, a disorder associated with systemic amyloidosis, a disorder associated with localized amyloidosis, a prion disease and/or a polyglutamine disorder.

68. The use of claim 67, wherein said neurodegenerative disease is selected from the group consisting of Alzheimer's disease, Huntington's disease and Parkinson's disease.

69. The use of claim 67, wherein said disorder associated with systemic amyloidosis is selected from the group consisting of Multiple myeloma, Chronic inflammatory disease, Rheumatoid arthritis, Tuberculosis, Skin abscess, lung abscess, Cancer, Hodgkin's disease, Hemodialysis for chronic renal failure, Heredofamilial amyloidosis, Familial Mediterranean Fever and Familial amyloid polyneuropathy.

70. The use of claim 67, wherein said disorder associated with localized amyloidosis is selected from the group consisting of Senile cardiac amyloidosis, Senile cerebral amyloidosis, Endocrine tumors, Medullary carcinoma of thyroid, Type II diabetes and Pancreatic islets β -cells.

71. The use of claim 67, wherein said prion disease is selected from the group consisting of Creutzfeldt-Jakob disease (CJD), spongiform encephalopathies (TSE's), mad cow disease, Gerstmann-Straussler-Scheinker disease (GSS) and Kuru.

72. The use of claim 67, wherein said polyglutamine disorder is selected from the group consisting of Huntington's disease (HD), Spinal and Bulbar Muscular Atrophy (SBMA), DentatoRubral and PallidoLuysian Atrophy (DRPLA), spinocerebellar ataxia type 1 (SCA1), spinocerebellar ataxia type 2 (SCA2), Spinocerebellar ataxia type-3 (SCA3; Machado-Joseph Disease), Spinocerebellar ataxia type 7 (SCA7) and Spinocerebellar ataxia type 17 (SCA17).

73. The use of claim 65, wherein said amyloid is a protein selected from the group consisting of Transthyretin, Amyloid beta protein, Procalcitonin, IAPP (Amylin), amyloid light chain (AL), non-immunoglobulin amyloid associated (AA), non-immunoglobulin amyloid associated serum precursor (SAA), α -synucleic protein, ataxin and huntingtin.

74. The use of claim 65, wherein said BChE derived peptide is set forth by SEQ ID NO:1.

75. The use of claim 65, wherein said medicament is providable at a dose range of 0.1 – 1000 micromol per kg body weight.

76. The use of claim 65, wherein said medicament is providable at a dose range of 1-100 micromol per kg body weight.

77. The use of claim 65, wherein said medicament is providable at a dose range of 5-50 micromol per kg body weight.